



INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference N.86941A JCI	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/GB 03/04749	International filing date (day/month/year) 05.11.2003	Priority date (day/month/year) 06.11.2002
International Patent Classification (IPC) or both national classification and IPC G01N33/50		
Applicant ISIS INNOVATION LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
 - ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:
 - I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

Date of submission of the demand 07.06.2004	Date of completion of this report 14.01.2005
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International application No. **PCT/GB 03/04749**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-37 as originally filed

Claims, Numbers

1-22 as originally filed

Drawings, Sheets

1/6-6/6 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

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5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).
- (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- ☐ the entire international application,
 - ☒ claims Nos. 12-14 (with respect to industrial applicability)
because:
 - ☒ the said international application, or the said claims Nos. 12-14 (with respect to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):
see separate sheet
 - ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
 - ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 - ☐ no international search report has been established for the said claims Nos.
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- ☐ the written form has not been furnished or does not comply with the Standard.
 - ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-14, 17-21
	No: Claims	22
Inventive step (IS)	Yes: Claims	1-14, 17-21
	No: Claims	22
Industrial applicability (IA)	Yes: Claims	1-11, 18-21
	No: Claims	

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2. Citations and explanations

see separate sheet

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The following documents (D) are referred to in this report; the numbering will be adhered to the rest of the procedure:

D1: US-A-5492816

D2: Journal Medicinal Chemistry, 1996, Vol. 39, Pages 5215-5227

D3: International Journal of Psychophysiology, 2001, Vol. 41, Pages 93-100

SECTION I

1. The subject matter of claims 15-16 have been not been the subject of International Search, therefore they will accordingly not be subject of International Preliminary Examination (Rule 66.1(e) PCT).

SECTION III

2. Claims 12-14, 17 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

SECTION V

3. Novelty (Article 33(2) PCT)

- 3.1 The subject matter of claim 22 is anticipated by D1.

D1 (page 4, lines 41-51) describes the measurement of superoxide anion by means of luminol using any standard spectrophotometer ("chemiluminometer" according to claim 22)

- 3.2 The subject matter of claims 1-14 and 17-21 including a **psychological stressor** in methods for determining whether an individual is experiencing changed physiological status (claim 1), or for screening for a stress relieving drug (claim 12) or a method for testing the efficacy (claim 17) are not disclosed in the prior art documents.

4. Inventive Step (Article 33(3) PCT)

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D2 is considered as the closest prior art document. D2 (abstract; page 5227, left column, fourth paragraph) describes the effect of inhibitors on the PMA induced superoxide anion burst in neutrophils using a luminometer. Claims 1, 12 and 17 differ from D2 in they relate to psychological stressors in:

- method for determining changed physiological status (claim 1)
- method for screening a stress relieving drug (claim 12)
- method of testing the efficacy of a proposed stress-relieving treatment (claim 17)

The technical problem to be solved with respect to claim 1 would reside in finding an alternative way to assay the physiological status of an individual.

The skilled person, equipped with the knowledge of D2, would not be motivated to arrive at the subject matter of claim 1, despite that D3 learns that beside physiological stressors, mental stressors exist for increasing the superoxide anion production. However, the prior art does not show, that said stress exposure leads to **less** superoxide anion production *in vitro* after stimulation by an inducer compared to an unexposed control.

Therefore, claims 1-11 and 18-21 would appear to involve an inventive step and also claims 12-14, relating to methods of screening for compounds influencing the superoxide anion production of claims 1-11 and claim 17, relating to the efficacy of a proposed stress relieving treatment using a method in accordance to claims 2-11.

5. For the assessment of the present claims 12-14 and 17 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

In this context the passage "administering a test compound to an individual" or "exposing an individual to a psychological stressor" according to claims 12 and 17

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is considered to cover treatment by surgery and therefore is a method of treatment.